Functional topography of the corpus callosum as revealed by fMRI and behavioural studies of control subjects and patients with callosal resection

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A R T I C L E   I N F O

A B S T R A C T

The concept of a topographical map of the corpus callosum (CC), the main interhemispheric commissure, has emerged from human lesion studies and from anatomical tracing investigations in other mammals. Over the last few years, a rising number of researchers have been reporting functional magnetic resonance imaging (fMRI) activation in also the CC.

This short review summarizes the functional and behavioral studies performed in groups of healthy subjects and in patients undergone to partial or total callosal resection, and it is focused on the work conducted by the authors. Functional data have been collected by diffusion tensor imaging and tractography (DTI and DTT) and functional magnetic resonance imaging (fMRI), both techniques allowing to expand and refine our knowledge of the commissure. Neuropsychological test were also administered, and simple behavioral task, as imitation perspective and mental rotation ability, were analyzed. These researches added new insight on the topographic organization of the human CC. By combining DTT and fMRI it was possible to observe that the callosal crossing points of interhemispheric fibers connecting homologous primary sensory cortices, correspond to the CC sites where the fMRI activation elicited by peripheral stimulation was detected. In addition, CC activation during imitation and mental rotation performance was also reported.

These studies demonstrated the presence of specific callosal fiber tracts that cross the commissure in the genu, body, and splenium, at sites showing fMRI activation, consistently with cortical activated areas. Altogether, these findings lend further support to the notion that the CC displays a functional topographic organization, also related to specific behavior.

1. Introduction

The corpus callosum (CC) is the main interhemispheric commissure. It arises in the brain of placental mammals (Aboitiz and Montiel, 2003) as an elongated midline structure composed of 200–800 million horizontal interconnecting homotopical and heterotopical cortical areas (Innocenti, 1986). The mature CC contains myelinated (70%) and unmyelinated fibers (30%), glial cells (astrocytes and oligodendrocytes), and neurons (Malobabić et al., 1984; Riederer et al., 2004; Revishchin et al., 2010; Rockland and Nayyar, 2012; Barbaresi et al., 2014). The human CC has been divided into five anatomical regions, which include from front to back the genu, the rostrum, the body or trunk—often subdivided into anterior, middle and posterior body—the isthmus, and the splenium (Fig. 1). Since there are no clear borders between regions, a variety of methods based principally on geometric criteria have been

proposed to define subregions (Witelson, 1989; Hofer and Frahm, 2006; Hofer et al., 2008; Chao et al., 2009).

1.1. Morphological structure of the corpus callosum

The anterior half of the human CC (genu, rostrum and anterior/central body) contains fibers interconnecting frontal association cortical areas. The posterior body mostly contains primary motor, somatosensory, and isthmus auditory fibers. In the splenium, primary visual and association temporo-occipital and parietal commissural fibers are mixed, forming a single segment with the hippocampal commissure through which parahippocampal fibers cross (Raybaud, 2010).

The different callosal regions have different fiber compositions: large diameter fibers have been described in the posterior part of the body, in the isthmus and in the splenium (Aboitiz et al., 1992; Aboitiz and

Montiel, 2003); small fibers are found in the rostrum, genu and anterior body (Aboitiz et al., 1992; Aboitiz and Montiel, 2003). Large diameter fibers (3–5 μm) in the posterior body and isthmus connect motor, somatosensory, and auditory cortices, exchanging information at high speed (Aboitiz et al., 1992; Raybaud, 2010); those in the posterior splenium connect at high speed visual cortices; small fibers (<0.4 μm) in the genu and anterior splenium connect high-order prefrontal and temporo-parietal associative areas. These observation received further support by very recent study in which the axonal radius and myelination have been estimated in the human CC, producing results consistent with histological findings (Oliveira et al., 2022). It has recently been shown that the length of large diameter fibers increases proportionally with the brain size or less during evolution, allowing to keep high speed connectivity (Yang et al., 2022). On the other hand, the length of smaller fibers increases proportionally more than the brain side, resulting in a higher conduction delay (Yang et al., 2022).

Fig. 1. Subdivisions of the human corpus callosum. Midsagittal magnetic resonance image of the corpus callosum (above) and its subdivision in seven anatomical regions according to a modified version of Witelson geometrical scheme (1989): here the orizontal line is the bicommissural line, not the line connecting the anterior- and posterior-most point of the CC. Region 1: Rostrum; 2: Genu; 3: Anterior midbody; 4: Central midbody; 5: Posterior midbody; 6: Isthmus; 7: Splenium. Both images are oriented in the Talairach space (Talairach and Tournoux, 1988), where the origin of X, Y and Z axes coincides with the anterior commissure (coordinates 0, 0, 0). From Fabri et al., 2014).

Neurons giving rise to callosal fibers lie in cortical layers III, V and VI. The vast majority of these fibers release excitatory amino acids (glutamate and/or aspartate) as neurotransmitters (Barbaresi et al., 1987); however, a small proportion of callosal neurons in cat and rat have been shown to release the inhibitory neurotransmitter GABA (Gonchar et al., 1995; Fabri and Manzoni, 2004; Higo et al., 2009).

1.2. Function of the corpus callosum

The function of the CC has been investigated for centuries, since from the 16th. Believed for long time to be the "seat of the soul" (Manzoni, 1998), it took until the 18th century to describe bundles of axons passing through the callosal white matter (WM) and connecting the two hemispheres (Manzoni, 2011). Its known functions include: interhemispheric exchange of information, integration of inputs reaching one or both hemispheres, facilitation of some, and inhibition of other cortical functions (Wahl et al., 2007; Koch et al., 2011; Innocenti et al., 2022). It has been shown that the size of the human CC positively correlates with intelligence (Einstein's CC was thicker than normal; Men et al., 2014) and that its integrity is essential for cognitive performances; thus CC resection and microstructural or developmental alterations are often associated with cognitive decline (O'Sullivan et al., 2001; Schulte et al., 2005; Paul, 2011; Passamonti et al., 2014; Westerhausen and Karud, 2018).

The earliest hypotheses on the function of the human CC came from studies of split-brain patients, subjects whose CC was partially or completely resected to prevent the diffusion of epileptic seizures (Gazzaniga, 2000, 2005). Patients with total or partial resection involving the posterior CC suffered from disconnection syndrome (Geschwind, 1965a, 1965b; Berlucchi, 2014) whereas in those with partial anterior resection the disconnection could be evidenced only by specific tests (Gordon et al., 1971; Berlucchi, 2012).

The emerging idea is that the CC connects the cerebral hemispheres and provides for interhemispheric integration and transfer of information. Also, from these studies, the idea of a functional topographical organization of the CC, corresponding to the morphological subdivisions above described, started to appear.

1.3. Functional topography of the corpus callosum

Ever since electrophysiological recordings demonstrating somatic sensory receptive fields in the anterior cat CC (Innocenti et al., 1972, 1974) and visual inputs to the splenium (Berlucchi et al., 1967; Hubel and Wiesel, 1967), the CC has been hypothesized to be topographically organized. Later, electrophysiological (Guillemot et al., 1987) and neuroanatomical findings (Pandya et al., 1971; Pandya and Seltzer, 1986), obtained by neural tracers injection, or selected cortical areas ablation in non-human primates, as well as findings from post-mortem investigations (De Lacoste et al., 1985), and studies of patients with surgical resection or callosal lesions (Caillé et al., 2005; Gazzaniga, 2005; Berlucchi, 2004), provided further support for the notion. This organization appears to give rise to modality-specific regions (Funnell et al., 2000), in which anterior callosal axons transfer motor information between the frontal lobes, and somatic sensory, auditory, and visual information is integrated by posterior fibers linking parietal, temporal and occipital lobes and crossing through the posterior midbody, isthmus and splenium, respectively.

A study of non-epileptic patients with transection of different portions of the anterior CC performed to remove cysts (Caillé et al., 2005) has confirmed the hypothesis by demonstrating that the middle part of the genu is involved in motor coordination and the anterior portion of the body in the transfer of simple somaesthetic information. Investigations of other sensory modalities have shown that the splenium is crucial for the interhemispheric transfer of visual (Gazzaniga and Freedman, 1973; see data and literature in Clarke et al., 2000) as well as auditory information (Sugishita et al., 1995; Pollmann et al., 2002).

The recent magnetic resonance imaging (MRI)-associated techniques, including functional MRI (fMRI), diffusion tensor imaging (DTI) and diffusion tensor tractography (DTT) are powerful methods to investigate the human brain in vivo. Over the past four decades these techniques enabled confirmation or rejection of earlier hypotheses about the functions of the CC and provided new insights on its functional organization. In non-human primates and other mammals they have also allowed to correlate data obtained by classic neuroanatomical techniques with DTI findings, and results of electrophysiological recordings with fMRI activation.

The callosal topography resulting from the application of DTI and DTT techniques has thus been confirmed to be in line with that described in previous human studies. Fibers connecting prefrontal cortical areas have been seen to cross through the anterior part of the CC; those connecting premotor and motor cortical areas cross at the level of the central callosal body (Abe et al., 2004; Huang et al., 2005; Hofer and Frahm, 2006; Zarei et al., 2006; Wahl et al., 2007; Chao et al., 2009); fibers connecting parietal cortical areas cross through the posterior callosal body, and those from occipital areas at level of the splenium (see also Dougherty et al., 2005; Shimony et al., 2006). Moreover, the hypothesis of a topographic organization of the CC as emerging from previous neuroanatomical (axonal degeneration and tract-tracing) animal studies and human lesion and post-mortem investigations has been confirmed by these studies. Slight differences have been demonstrated between human and monkey topographic organization in relation to the much greater expansion of the human frontal cortex.

In recent years an increasing number of fMRI studies have described WM activation in the anterior CC during behavioral tasks involving interhemispheric transfer (Tettamanti et al., 2002; Omura et al., 2004; Weber et al., 2005; Mazerolle et al., 2008, 2010) as well as during voluntary swallowing, which is not a specific interhemispheric transfer task (Mosier and Bereznaya, 2001). A blood oxygen level dependent (BOLD) effect was also detected in the posterior callosal region (isthmus and splenium) during an interhemispheric transfer task that was based on visuomotor stimuli and responses requiring that information cross the CC for a behavioral response to be elicited ("crossed condition"; Mazerolle et al., 2008, 2010). The anterior CC has been seen to be involved in transferring information between prefrontal and premotor regions, and the posterior CC in information transfer between parietal, occipital and temporal cortices (Stancak et al., 2000; Zarei et al., 2006; Bonzano et al., 2008; Meyer et al., 1995).

This paper collects the neuropsychological and imaging studies carried out by the author's group and co-workers on split-brain patients, contributing to define the functional organization of the CC. The research on split-brain patients may provide a significant contribution to the understanding the role and organization of the CC. In particular, by comparing results from total and partial callosotomized patients and with control subjects, many findings have been obtained on the organization and functions of the commissure.

The behavioral and functional data here reported were collected in different studies during the last twenty-five years, from healthy adult volunteers and from callosotomized patients. Patients' data and extent of callosal resection are shown in Table 1 and in Fig. 2, respectively. The related neuropsychological and functional studies are listed in Table 2. Table 3 evidenced the participation of each patient in different studies.

Neuropsychological studies were carried out investigating the role of CC in the following functions.

1. Interhemispheric transfer of different kind of sensory stimuli (touch, taste, auditory);
2. Interhemispheric coordination of motor responses;
3. Allocation of attention and learning functions;
4. Hemispheric collaboration in higher brain functions;
5. Emotional hemispheric specialization.

Shortly later, a functional research topic emerged from research on

Table 1
Data of patients participating in the studies described.

Code	Gender	I.Q	Oldfield score (Oldfield, 1971)	Age at the time of last study	Age at surgery (years)	Callosal resection
P1*§	M	90	13	50	33	total
P2	M	81	10	49	22	total
P3	M	83	21	39	19	total
P4	F	93	13	57	31	total
P5	F	70	14	37	16	total
P6	F	70	10	44	26	total
P7	M	88	10	52	42	3/4 post
P8	F	92	11	59	31	4/5 ant
P9	M	70	46	45	19	3/4 ant
P10	M	87	10	49	28	3/4 ant
P11	M	70	10	45	21	3/4 ant
P12	F	70	12	40	15	2/3 ant
P13	F	70	10	24	20	2/3 ant
P14	M	82	45	26	21	3/4 ant
P15	M	70	12	46	38	3/4 ant
P16	M	80	14	49	46	2/3 ant
P17	M	80	10	55	36	1/3 ant
P18	M	98	10	26	23	central
P19*	F	99	10	50	26	4/5 ant
P20*	F	86	12	57	33	3/4 ant
P21*	F	70	16	53	29	3/4 ant

*patient carrying a metallic clip in the brain.
§ deceased on 2007, at 56 years.

this group of patients, in whom for the first time the functional MRI technique was employed to study the pattern of cortical activation evoked by simple sensory stimulation in split-brain patients.

2. Neuropsychological studies

2.1. Interhemispheric transfer of sensory stimuli

2.1.1. Interhemispheric transfer of sensory stimuli: touch

Neuropsychological tests evaluating interhemispheric tactile transfer were administered to one patient before and after the second callosotomy resecting the posterior portion of CC (Fabri et al., 2001), and later to some patients with different degree of callosal resection (Fabri et al., 2005).

Before posterior callosotomy, the first patient was able in 100% of trials to name the familiar objects explored with either hand (Tactile Naming Test; TNT), to state whether the object explored with one hand was the same or a different object from that explored with the other hand (Same Different Recognition Test; S-DRT), and to localize with the thumb the points on fingers 2–5 touched by the experimenter in the same (Tactile Finger Localization Test; TFLT, intramanual mode) or in the contralateral (TFLT, intermanual mode) hand. The patient's post-operative performance in the TNT was as correct as preoperatively with the right hand, but failed with the left hand in 89% and 84% of trials after six and twelve months, respectively. Also performance in the S-DRT was very poor, with correct responses well below chance in both postoperative sessions. In the TFLT, performance was as high as pre-operatively in the intramanual mode with both hands, without errors six months after surgery, and with few errors after one year. On the contrary, in the intermanual mode he made errors in 82% of trials in the right-to-left transfer and in 83% in the opposite direction after six months; after one year errors were 85% and 79%, respectively. This case provides direct demonstration that interhemispheric transfer of tactile information requires the integrity of the posterior body of the CC, through which somatosensory interhemispheric fibres cross the commissure (Fabri et al., 2001).

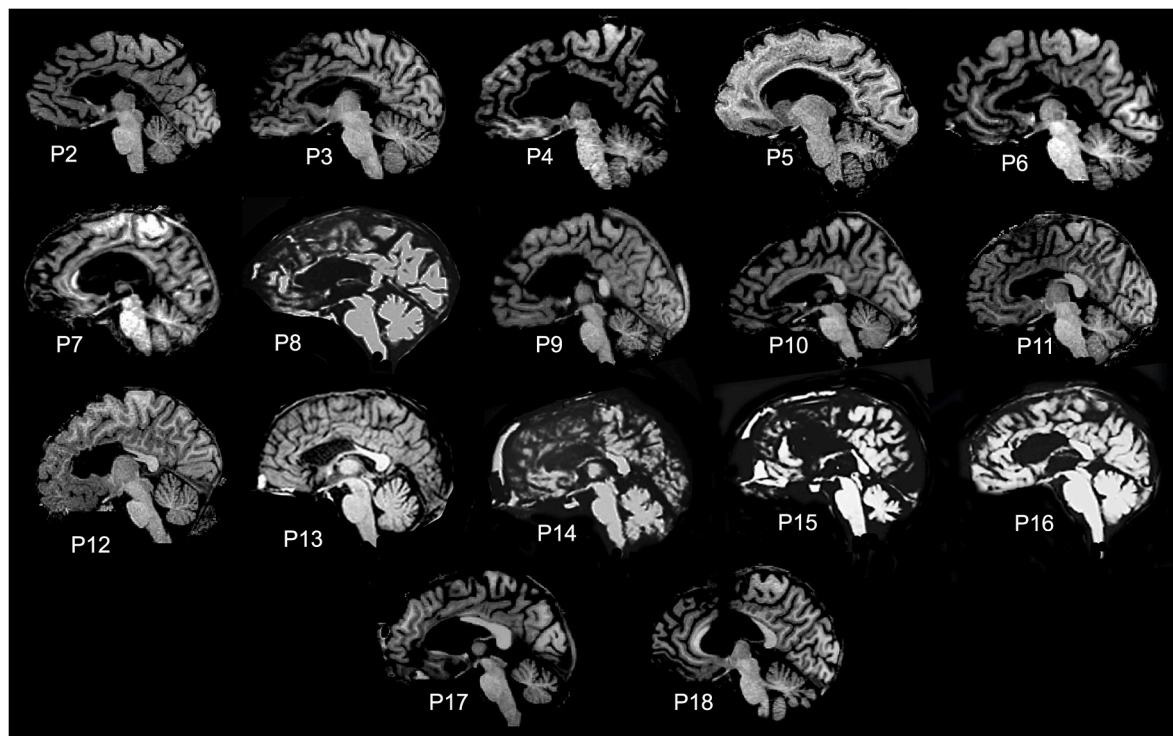Three subjects of the second group performed well with both hands

Fig. 2. Midsagittal MR images from callosotomy patients participating in the studies described, showing the extent of callosal resection. Patients P2–P6 underwent to a total callosotomy. Patient P7 shows a posterior resection. Patients P8–P17 display an anterior callosotomy of various extent. Finally, patient P18 has a central callosal resection. Images from patients P1 (total callosotomy), and P19–P21 (anterior callosotomy) are not showed since these patients could not be submitted to MRI because of a metallic arterial clip in their brain. Anterior pole on the left.

Table 2
Behavioral and functional studies in which patients participated.

	Authors	Title	Kind of study	Patients involved
1	Fabri M, Polonara G, Quattrini A, Salvolini U, Del Pesce M, Manzoni T. 1999. Eur J Neurosci 11: 3983–3994.	Role of the corpus callosum in the somatosensory activation of the ipsilateral cerebral cortex: a fMRI study of callosotomized patients.	Functional	P2, P3, P4, P5, P6, P8, P9, P10, P11, P13, P14, P15, P16.
2	De Guise E, Del Pesce M, Foschi N, Quattrini A, Papo I, Lassonde M. 1999. Brain 122: 1049–1062.	Callosal and cortical contribution to procedural learning.	Neuropsychological	P3, P4, P10.
3	Arguin M, Lassonde M, Quattrini A, Del Pesce M, Foschi N, Papo I. 2000. Neuropsychologia 38: 283–291.	Divided visuo-spatial attention systems with total and anterior callosotomy.	Neuropsychological	P1, P2, P3, P9, P10, P12, P13, P14 P19, P20.
4	Aglioti SM, Tassinari G, Fabri M, Del Pesce M, Quattrini A, Manzoni T, Berlucchi G. 2001. Eur J Neurosci 13: 195–200.	Taste laterality in the split brain.	Neuropsychological	P1, P7.
5	Fabri M, Polonara G, Del Pesce M, Quatttrini A, Salvolini U, Manzoni T. 2001. J Cogn Neurosci 13: 1071–1079.	Posterior corpus callosum and interhemispheric transfer of somatosensory information: a fMRI and neuropsychological study of a partially callosotomized patient.	Neuropsychological and Functional	P7.
6	Corballis MC, Corballis PM, Fabri M. 2003. Neuropsychologia 42: 71–81.	Redundancy gain in simple reaction time following partial and complete callosotomy.	Neuropsychological	P3, P7, P9, P13.
7	Hausmann M, Corballis MC, Fabri M. 2003. Neuropsychology 17: 602–609.	Line bisection in the split brain.	Neuropsychological	P3, P7, P9, P13.
8	Fabri M, Del Pesce M, Paggi A, Polonara G, Bartolini M, Salvolini U, Manzoni T. 2005. Cogn Brain Res 24: 73–80.	Contribution of the posterior corpus callosum to interhemispheric transfer of tactile information.	Neuropsychological	P2, P3, P4, P10, P11, P13.
9	Hausmann M, Corballis MC, Fabri M, Paggi A, Lewald J. 2005. Cogn Brain Res 25: 537–546.	Sound lateralization in subjects with callosotomy, callosal agenesis, or hemispherectomy.	Neuropsychological	P2, P19.
10	Ouimet C, Jolicoeur P, Miller J, Ptito A, Paggi A, Foschi N, Ortenzi A, Lassonde M. 2009. Neuropsychologia 47: 684–692.	Sensory and motor involvement in the enhanced redundant target effect: a study comparing anterior- and totally split-brain individuals.	Neuropsychological	P1, P2, P5, P10, P11, P19, P20.
11	Ouimet C, Jolicoeur P, Lassonde M, Ptito A, Paggi A, Foschi N, Ortenzi A, Miller J. 2010. Neuropsychologia 48: 3802–14.	Bimanual crossed-uncrossed difference and asynchrony of normal, anterior- and totally-split-brain individuals.	Neuropsychological	P1, P2, P5, P10, P11, P19, P20.
12	Pizzini FB, Polonara G, Mascioli G, Beltramello A, Moroni R, Paggi A, Salvolini U, Tassinari G, Fabri M. 2010. Brain Res 1312: 10–17.	Diffusion tensor tracking of callosal fibers several years after callosotomy.	Functional	P2, P3, P6, P7, P10.
13	Miller MB, Sinnott-Armstrong W, Young L, King D, Paggi A, Fabri M, Polonara G, Gazzaniga MS. 2010. Neuropsycologia 48: 2215–2220.	Abnormal moral reasoning in complete and partial callosotomy patients.	Neuropsychological	P2, P9, P10, P12.
14	Fabri M, Polonara G. 2013. Neural Plast. https://doi.org/10.1155/2013/251308. Epub 2013 Feb 14.	Functional topography of the human corpus callosum: a fMRI mapping study.	Functional	P7, P8, P9, P12, P17, P18.
15	Polonara G, Mascioli G, Foschi N, Salvolini U, Pierpaoli C, Manzoni T§, Fabri M*, Barbaresi et al., 2014. J Neuroimaging. https://doi.org/10.1111/jon.12136.	Further evidence for the topography and connectivity of the corpus callosum: a fMRI study of patients with partial callosal resection.	Functional	P7, P8, P9, P12, P17, P18
16	Prete G, Laeng B, Fabri M, Foschi N, Tommasi L. 2015a. Neuropsychologia 68: 94–106.	Right hemisphere or valence hypothesis, or both? The processing of hybrid faces in the intact and callosotomized brain.	Neuropsychological	P10.
17	Prete G, D'Ascenzo S, Laeng B, Fabri M, Foschi N, Tommasi L. 2015b. J Neuropsychol 9: 45–63.	Conscious and unconscious processing of facial expressions: Evidence from two split-brain patients.	Neuropsychological	P3, P10.
18	Pierpaoli C. Foschi N, Cagnetti C, Ferrante L, Manzoni T†, Polonara G, Fabri M. 2018. Arch Ital Biol 156: 12–26.	Imitation strategies in callosotomized patients.	Neuropsychological	P2, P3, P5, P7, P9, P11, P12, P17, P18, P19, P20, P21.
19	Pierpaoli C, Ferrante L, Foschi N, Lattanzi S, Sansonetti R, Polonara G, Mari M, Nardi B, Fabri M. 2020. Symmetry 12: 1137.	Mental rotation ability: right or left hemisphere competence? What we can learn from callosotomized patients and psychotic patients.	Neuropsychological	P2, P3, P4, P5, P9, P10, P11, P17, P19.
20	Pierpaoli C, Foschi N, Fabri M, Polonara G. 2021. J Syst Integr Neurosci 2021. doi: 10.15761/JSIN.1000253	Cortical activation during imitative behavior: a fMRI study in callosotomized patients.	Functional	P2, P3, P9, P10, P11, P17.
21	Pierpaoli C, Ombrosi M, Ghoushi M, Foschi N, Lattanzi S, Polonara G, Fabri M. 2021. Symmetry 13: 1953.	Cortical activation in mental rotation: observations in healthy subjects and split-brain patients.	Functional	P2, P3, P4, P5, P9, P10, P11, P12, P17.

in the TNT (mean 93% and 95% of correct responses for the right and the left hand, respectively). One had an intact splenium and PCB, while in the other two the splenium and probably part of the trunk of the CC were spared. These patients also provided 95–100% of correct answers in the S-DRT and 77%–100% in the intra- and intermanual TFLT tasks with both hands, denoting interhemispheric exchange of tactile information (Fabri et al., 2005). The other patients, with total resections, performed well in the TNT with the right hand (93% of correct responses), but poorly with the left (mean: 30% of correct responses). Performance in the S-DRT was highly variable, with correct responses ranging from 50% to 100%. However, the results from this total split-brain patients were overall significantly poorer than those obtained in the partial callosotomy ones. In the TFLT, the three complete callosotomy patients gave 100% of correct answers with both hands in the intramanual task; in the intermanual task correct responses were 78%–93% with the right hand and 67%–90% with the left. Although these values are above chance

(=12.5%), differences from the results of partially callosotomized patients are statistically significant. These data indicate that somatosensory information from the left hand reached the speaking hemisphere (very likely the left, all patients having high right-handedness scores), probably along the fibres crossing the posterior region of the CC body.

2.1.2. Interhemispheric transfer of sensory stimuli: taste

The projection of taste information from each side of the tongue to the gustatory cortex has been reported to be uncrossed in some studies and crossed in other studies (see data and literature in Mascioli et al., 2015). Previous data from a complete callosotomy patient (Aglioti et al., 2000), showed that he was able to verbally identify basic taste stimuli applied to either side of the tongue, though his accuracy and speed of performance were significantly better for left than for right hemitongue stimuli, a difference absent in normal controls. Two out of the callosotomy patients with bilateral anatomical integrity of the cortical taste

Table 3

Overview of participation of each patient in the different studies, listed in Table 2.

Code	Studies in which patients participated																				
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
P1[a] [b]			x	x						x											
P2	x		x					x	x	x	x	x	x					x	x	x	x
P3	x	x	x				x	x									x	x	x	x	x
P4	x	x						x											x		x
P5	x									x	x							x	x		x
P6	x											x									
P7				x	x	x	x					x		x	x			x			
P8	x													x	x						
P9	x					x	x							x	x			x	x	x	x
P10	x	x	x					x		x	x	x	x			x	x	x	x	x	x
P11	x							x		x	x							x	x	x	x
P12			x											x	x			x			x
P13	x		x			x	x	x													
P14	x		x																		
P15	x																				
P16	x																				
P17			x										x	x	x			x	x	x	x
P18														x	x			x			
P19*			x						x	x	x							x	x		
P20*			x							x	x							x			
P21*																		x			

[a] Patient carrying a metallic clip in the brain.
[b] Deceased on 2007, at 56 years.

areas participated in a subsequent study (Aglioti et al., 2001). The two patients, one with a complete CC resection, the other sparing the genu and the rostrum, were tested for discrimination of three basic taste stimuli (sour, bitter, salty) applied to either side of the tongue. In both patients, response accuracy was significantly above chance for both hemitongues but there was a significant advantage for the left side. Reaction time was shorter for left stimuli than for right stimuli but the difference was not significant. The results confirm and extend previous findings in another callosotomy patient, indicating that taste information from either side of the tongue can reach the left hemisphere in the absence of the CC, and that the ipsilateral input from the tongue to the left hemisphere is functionally more potent than the contralateral one.

2.1.3. Interhemispheric transfer of sensory stimuli: auditory

The question of whether there is a right-hemisphere dominance in the processing of auditory spatial information in human cortex as well as the role of the CC in spatial hearing functions is still a matter of debate. Here, this issue was approached by investigating two late-callosotomized subjects using a task of sound lateralization with variable interaural time differences. Besides a significant reduction in their acuity, subjects with total or partial callosal resection exhibited a considerable leftward bias of sound lateralization compared to normal controls. The results indicated that the integrity of the CC is not indispensable for preservation of sound-lateralization ability. On the other hand, transcallosal interhemispheric transfer of auditory information obviously plays a significant role in spatial hearing functions that depend on binaural cues. This is in accordance with the finding that the auditory cortices are interconnected primarily via the posterior midbody (Hausmann et al., 2005).

2.2. Interhemispheric coordination of motor responses

Subjects lacking the CC usually show impairments on tasks requiring bilateral interdependent motor control. However, few studies have assessed the ability of these subjects to learn a skill that requires the simultaneous contribution of each hemisphere in its acquisition.

Since the CC links cortical areas of both hemispheres, including the dorsolateral frontal areas, the study of interhemispheric integration and transfer of a visuomotor procedural skill in patients, whose interhemispheric communication was interrupted, provided an interesting model

for the investigation of the cortical systems involved in this kind of memory. Furthermore, considering the importance of the CC in bimanual co-ordination, the specific role of this structure in motor learning could be defined. Three adult patients participated in a study investigating whether they could learn a visuomotor skill that involved a motor control from either one or both hemispheres (De Guise et al., 1999). None of the patients was able to learn the task in the bimanual condition. Patients with frontal epileptic foci also failed to learn the task in the unimanual condition when they were using the hand contralateral to the damaged hemisphere (De Guise et al., 1999). All other subjects, including the callosotomized patients with temporal foci, learned the visuomotor skill as well as their controls in the unimanual condition. In spite of the absence of transfer and interhemispheric integration of procedural learning, some of the callosotomized patients were able to learn the sequence explicitly. In summary, the results of this study suggest that the anterior part of the CC, which connects the frontal lobes, is crucial for integration and transfer of a procedural visuomotor skill.

2.3. Allocation of attention and learning-memory functions

Another "higher function" in which the CC might be involved is the attentive capacity. Four patients, three with total and one with anterior callosotomy participated in a study investigating the role of the CC in the inter-hemispheric integration of visuo-spatial attention system (Arguin et al., 2000). Subjects produced simple reaction times to visual targets shown to the left or right visual hemifield. The results indicate that most split-brain subjects, in contrast to normal subjects, are capable of directing their attention to left and right visual field locations simultaneously and independently, and therefore that each cerebral hemisphere controls its own visuo-spatial attention mechanism. This results from split-brains contrasts with evidence from normal subjects, who are incapable of dividing their attention across two distinct spatial locations at the same time (Arguin et al., 2000). These results therefore assign a crucial role to the CC, both anterior and posterior, in the functional integration of the brain areas of each hemisphere that are involved in the orientation of visuo-spatial attention.

2.3.1. Line bisection

A role for the posterior CC, likely the splenium, was strongly suggested also in the processing of visual inputs, in a study examining the

line bisection performance in four patients with resection of the CC (one total, one partial posterior and two partial anterior; Hausmann et al., 2003). All subjects were instructed to bisect horizontal black lines, presented on a white sheet of paper, into two parts of equal length by marking the subjective midpoint of each line with a fine pencil. All participants completed the task with one hand and then repeated it with the other in a balanced order. The control participants showed a leftward bias, especially with the left hand, implying right-hemispheric dominance in spatial attention. Two patients with anterior callosotomy showed similar biases, suggesting that the anterior CC plays only a small role. The patient with complete callosotomy showed a strong right bias, regardless of hand used. The patient with posterior callosotomy showed the opposite pattern: a strong left bias, regardless of hand used. These data suggest that the posterior CC normally plays a role in line bisection and that its resection produces consistent bias, the direction of which depends on the hemisphere assuming control.

2.4. Hemispheric collaboration in higher brain functions

This line of research deals with the ability of imaging oneself in another's shoes. This function has been ascribed mainly to the right hemisphere, and therefore a correct performance is supposed to require hemispheric cooperation.

Recent functional neuroimaging studies indicate that processes for attributing beliefs and intentions to other people are lateralized to the right temporal parietal junction (TPJ; see literature in Miller et al., 2010), which activity in the right hemisphere, but not the left, is correlated with moral judgments of accidental harm. These findings suggest that patients with disconnected hemispheres would provide abnormal moral judgments on accidental harm and failed attempts to harm, since normal judgments in these cases require information about beliefs and intentions from the right brain to reach the judgmental processes in the left brain. The study examined this hypothesis by comparing the performance of 22 normal subjects to four split-brain patients, one with the complete CC resection, one with central, and two with anterior resection (Miller et al., 2010). Patients and controls made moral judgments about scenarios, in each of them the agent's action either caused harm or not, and the agent believed that the action would either cause harm or not. The crucial scenarios involved accidental harm (where the agent falsely believed that harm would not occur, but the outcome was harmful) and failed attempts (where the agent falsely believed that harm would occur, but the outcome was not harmful). For the patients, this testing did not require any lateralized procedures as only the left hemisphere was assumed to verbally respond. Previous studies show that normal subjects typically base their moral judgments on agents' beliefs even when these are inconsistent with the actions' outcomes (see literature in Miller et al., 2010). It was found that all patients based their moral judgments primarily on actions' outcomes, disregarding agents' beliefs. The study demonstrated that full and partial callosotomy patients fail to rely on agents' beliefs when judging the moral permissibility of those agents' actions. This finding confirms the hypotheses that specialized belief-ascription mechanisms are lateralized to the right hemisphere and that disconnection from those mechanisms affects normal moral judgments. Moreover, the neural mechanism by which interhemispheric communication occurs between key left and right hemisphere processes seems complex. Since the partial anterior callosotomy patients also showed the effect, it would appear the right TPJ calls upon right frontal processes before communicating information to the left speaking hemisphere.

2.4.1. Anatomical imitation
A similar function is the strategy adopted in imitating intransitive gestures performed by a model in a third person perspective, which likely requires a mental rotation operation.

The imitation is a behavioral event reproducing observed actions; it allows individuals to establish the first form of relationship between infants and parental figures, and it is basic for learning. In everyday life, the actions to be imitated are generally presented with the imitator facing the model, i.e., in third person perspective. Here recent studies focused on the anatomical perspective taking in imitating intransitive meaningful gestures, and on its relationship with the CC are described (Pierpaoli et al., 2014, 2018).

When invited to imitate actions of someone facing them, individuals can act in two ways: either in an anatomical mode, activating exactly the same effectors as the model (hence the same nervous mechanisms); or in a specular (mirror) mode, activating the effectors sharing an external spatial reference with those activated by the model (see literature in Fabri et al., 2021).

In the above-mentioned studies, participants' responses produced enlightening results: both groups used the mirror perspective when free to imitate, but only the control group (with intact CC) used the anatomical perspective when asked to use the *same* limb. This lays for split-brain patients to differently encode for the *same* concept, or not to be able to translate the *same* concept into a motor schema based on anatomical criteria. Observations on callosotomy subjects seem to point to a difference from control subjects, thus suggesting that some high order abstract functions require hemispheric cooperation (Pierpaoli et al., 2018).

2.4.2. Mental rotation ability
Mental rotation is an abstract operation whereby a person imagines to rotate an object or a body part to place it in a different position. Mental rotation is strictly concerned with anatomical imitation, as suggested in previous behavioral studies. It has been hypothesized that the different performances of the split-brain patients' group respect to the controls in the imitative performance could be possibly due to an impaired capacity for mental rotation, in which the CC might have a role. Assuming the existence of a causal link between callosal fibers functionality and the anatomical imitation performance, the mental rotation ability was investigated in the same groups of subjects previously tested, i.e., patients with partial or total resections of the CC, and healthy adults with intact CC.

The results from behavioral studies (Pierpaoli et al., 2020b) demonstrated that control subjects performed mental rotation almost perfectly, both with the model in first and in third person perspective. Callosotomized patients showed some impairment, mainly when the model was in 3rd person. The results indicated the central role of interhemispheric connections in mental rotation, in particular the anterior portion (Pierpaoli et al., 2020b). These behavioral data all agree in the observation that, concerning egocentric transformation, back orientation (first person presentation) produces better performances than front orientation (third person presentation).

2.5. Emotional hemispheric specialization

A recent study, designed to disentangling the two accounts for right hemisphere and/or valence hypotheses, was carried out by presenting to healthy participants and to one patient with anterior callosotomy (P10) 'hybrid faces' (Prete et al., 2015a). All participants were asked to judge the friendliness level of stimuli, which is an indirect measure of the processing of emotional information, despite this remaining "invisible". This study confirmed that the low spatial frequencies of emotional faces influence the social judgments of observers. In the light of the results obtained in the callosotomized patient, the two main hypotheses in emotion processing could be considered as complementary rather than competing, at least in the case of implicit emotion processing. In particular, it can be hypothesized that the right hemisphere is clearly dominant when more than one subliminal emotional 'unit' have to be processed at the same time, thus suggesting the coexistence of both types of cerebral organization for processing of subliminal emotion, i.e., the emotional content of facial expression due to the low spatial frequencies. Therefore, the right hemisphere and the valence accounts are not

mutually exclusive, at least in the case of subliminal emotion processing (Prete et al., 2015a). In addition, the partial anterior callosal resection does not seem to modify the patient's performance respect to controls, thus suggesting that the anterior CC is not involved in this particular function.

Another issue analyzed was the relation between hemispheric specialization and processing of explicit and implicit facial expressions of emotion, assuming a right-hemispheric superiority in detecting both positive and negative emotions (Prete et al., 2015b). Two split-brain patients (one with total and one with partial anterior resection) and a group of healthy participants were tested using tachistoscopic stimuli consisting of hybrid or implicit/explicit expressive faces, presented both centrally and bilaterally (in this case, the facial expressions presented in the left and right hemifields could be either identical or different). All participants were asked to evaluate the friendliness level of faces. When the expressions were shown explicitly, the control group and the partially callosotomized patient based their judgment on the face shown in the LVF (to the right hemisphere); the complete split-brain patient based his ratings mainly on the face presented in the right visual field, i. e., to the left hemisphere. It can be concluded that the processing of implicit emotions does not require the integrity of callosal fibres and can take place within subcortical routes lateralized in the right hemisphere. The results obtained seem to suggest that both the hemispheres can process subliminal expressions, but the social judgments they attribute to these stimuli is different, revealing a right-hemispheric superiority in emotion processing (Prete et al., 2015b). In addition, also in this case, the partial anterior callosal resection does not seem to modify the patient's performance respect to controls, thus suggesting that the anterior CC is not involved in this particular function. On the contrary, the total callosotomy patient performed differently from controls, indicating that the posterior CC has some role in the emotion processing and evaluation.

The overall results from these neuropsychological studies indicate different functions for the different CC regions, but the correspondence between the two remains necessarily rather approximate. A more precise association could be obtained in some cases in the functional studies.

3. Functional magnetic resonance imaging studies

Functional MRI studies were carried out investigating the role of CC in the following functions.

1. Interhemispheric transfer of different kind of sensory stimuli (touch, taste);
2. Activation of the CC by different sensory stimuli and simple motor task;
3. Hemispheres collaboration in higher brain functions.

In these cases, functional studies provided confirmation of a topographical organization of the CC by showing activation foci in different sites according to the different task.

3.1. Interhemispheric transfer of different kind of sensory stimuli

3.1.1. Interhemispheric transfer of different kind of sensory stimuli: touch
Functional fMRI was applied to control subjects and callosotomy patients to verify whether touch information transfer between the hemispheres occurs though axons crossing in the posterior CC (Fabri et al., 1999, 2001; Polonara et al., 2014).

The hypothesis has been confirmed by data obtained in subjects with callosal resection. In fMRI investigations of split-brain patients (Fabri et al., 1999, 2001) unilateral tactile stimulation of the hand activated only the contralateral somatosensory cortex if the resection involved the posterior callosal body (PCB), whereas it activated bilateral areas in patients who had an intact PCB, as it did in control subjects (Fabri et al., 1999). A combined neuropsychological and fMRI study (Fabri et al.,

2001; see above), conducted before and after resection of the PCB and splenium in a two-stage callosotomy patient, provided further evidence that interhemispheric transfer of tactile information is mediated by fibres running through the posterior part of the CC body, thus confirming that the posterior midbody is the tactual channel.

3.1.2. Interhemispheric transfer of different kind of sensory stimuli: taste
Functional fMRI was used for revealing activations in the human brain by lateralized tactile-gustatory stimulations of the tongue. Salt, a basic taste stimulus, and water, now recognized as an independent taste modality, were applied to either hemitongues with pads similar to the taste strips test for the clinical psychophysical evaluation of taste. With both stimuli, the observed cortical patterns of activations could be attributed to a combined somatosensory and gustatory stimulation of the tongue, with no significant differences between salt and water. Stimulation of each hemitongue evoked a bilateral activation of the anterior insula-frontal operculum, ascribable to the gustatory component of the stimulation, and a bilateral activation of the inferior part of the postcentral gyrus, due to the tactile component of the stimulation. The results are in line with the notion that the representation of the tongue in the cerebral hemispheres in both the touch and the taste modalities is bilateral. Clinical and brain stimulation findings indicate that this bilaterality depends primarily on a partial crossing of the afferent pathways, perhaps with a predominance of the crossed pathway in the touch modality and the uncrossed pathway in the taste modality. Previous behavioral evidence suggests that the CC is not indispensable for this bilateral representation, but it can contribute to it by interhemispheric transfer of information in both modalities. Little is known about the callosal connections of the gustatory cortices in humans, but DTI investigations performed on some of the participants to this study (Fabri and Polonara, 2013; Polonara et al., 2014) have tracked fibers running through the anterior CC and interconnecting the anterior insulae–frontal opercula of the two sides. In addition, an activation focus was observed in the anterior part of the CC during taste stimulation (Fig. 3A, B), strongly suggesting an exchange of interhemispheric messages between the taste cortical areas receiving ascending inputs.

3.2. Activation of the CC by different sensory stimuli and simple motor task

As reported above, data from the newer imaging techniques suggest that a hemodynamic response can also be evoked in the WM, particularly in the CC. These findings were at first observations sporadically recorded during interhemispheric transfer tasks performed by subjects within the magnet (Tettamanti et al., 2002; Omura et al., 2004; Weber et al., 2005; Mazerolle et al., 2008), or during activities not involving specific interhemispheric transfer tasks, such as voluntary swallowing (Mosier and Bereznaya, 2001). Moreover, a BOLD signal was elicited in isthmus and splenium (posterior CC) by a task based on the interhemispheric transfer and integration of visuo-motor information, where crossing of the CC is needed for a behavioral response to be elicited ("crossed condition"; Mazerolle et al., 2008). For long time it has been believed that the BOLD effect is mainly due to the metabolic activity associated with synaptic rather than spiking activity, and therefore it could be evoked only in gray matter (GM; Logothetis et al., 2001). Several studies have documented that information transfer between premotor and prefrontal areas involves the anterior CC, and transfer between parietal, occipital and temporal regions involves the posterior CC (Meyer et al., 1995; Stancak et al., 2000; Zarei et al., 2006; Bonzano et al., 2008).

These investigations, documenting CC functional activation during behavioral tasks, opened the way to re-examine fMRI studies on the cortical representation of gustatory, tactile, auditory and visual sensitivity and of motor activation in normal subjects for evidence of a functional callosal topography in healthy subjects and partially callosotomized patients.

Recently, additional evidence reported that the task-evoked BOLD signal in WM, although usually weaker than that evoked in GM, displays features demonstrating that it also is related to neural activity (Gore et al., 2019): it varies with the level of anesthesia exactly as the BOLD signals from cortical areas; the BOLD signal in WM can by modulated by stimulus parameters (i.e., intensity, frequency), in a corresponding way with GM. These observations provide further support to the notion that fMRI could be a valid means to study the topographical organization of the CC.

In a systematic study (Fabri et al., 2011) the BOLD effect evoked in the CC by simple sensory stimuli or by the performance of motor tasks activating the specific cortical areas were examined. Activation foci were consistently found in discrete CC regions in intact-brain subjects: anterior (taste stimuli), central (motor tasks), central and posterior (tactile stimuli), and splenium (visual stimuli) (Fig. 3, left panel). Preliminary report also showed activation in the most anterior CC by olfactory stimulation (not shown; Fabri et al., 2014). The study allowed to establish that a BOLD signal could be evoked in CC fibers and that the foci related to motor tasks and sensory stimuli agreed with the notion of a topographic organization. In subsequent years the peripheral sensory stimulation protocols applied in the earlier studies (Fabri et al., 2011) were administered to partial callosotomy patients (Polonara et al., 2014). In callosotomized patients, activation foci were present in spared CC different portions, accordingly with the specific kind of sensory or

motor stimulation. These results showed the extant CC portions displayed a BOLD signal, to provide additional evidence for the concept of a functional map in the CC. In the same study, DTI data were also obtained in callosotomy and control subjects, to determine whether tracts seeded from cortical areas activated by specific sensory stimuli co-localized with CC activation (Fig. 3, right panel).

The activation foci evoked by different sensory stimuli are found at different sites in the patients CC: patients with an intact anterior CC exhibited taste activated foci at the site where interhemispheric fibres from the gustatory areas crossed the CC. Foci elicited by tactile stimulation of the hand were detected in the middle and posterior body, where interhemispheric fibres arising from somatosensory areas were also observed. In one patient, a more anterior focus also was found, likely in the CC region where interhemispheric fibres from motor cortices cross through the commissure. This observation is consistent with previous findings obtained in healthy subjects (Fabri et al., 2011), where activation was often found the primary motor cortex after tactile stimulation (Polonara et al., 1999). Callosal foci elicited by visual stimuli were found in the splenium, as expected, and in the CC region harbouring interhemispheric fibres arising from occipital areas activated by visual stimulation.

The topographical CC map resulting from these studies was in line with human post-mortem data (De Lacoste et al., 1985), with studies of patients with CC injury or surgical resection (Volpe et al., 1982; Bentin
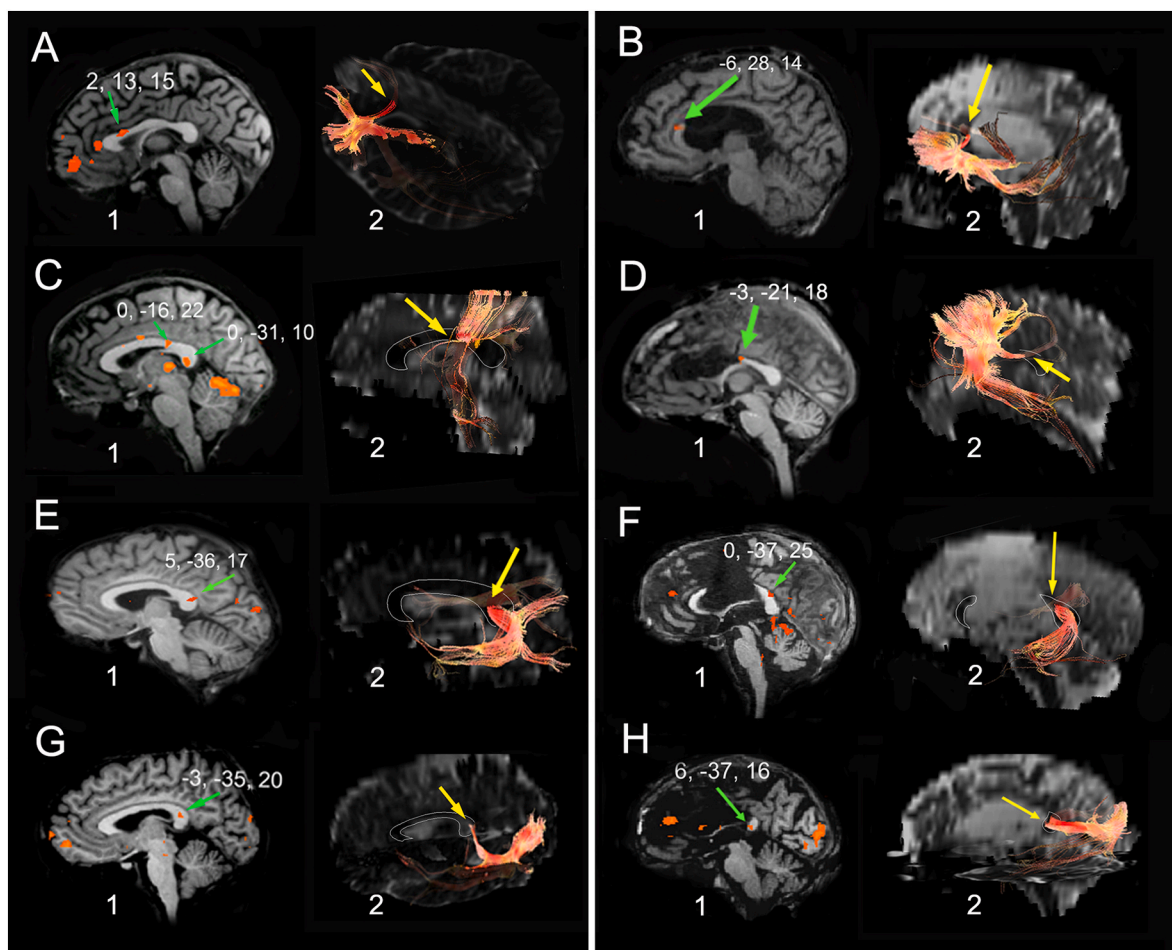

Fig. 3. Activation evoked in the CC by different peripheral sensory stimuli. Left panel: BOLD effect evoked in the CC of control subjects by gustatory, tactile, auditory and visual stimulation (respectively A1, C1, E1, G1, green arrows), and sites where fibres connecting fronto-opercular, parietal, temporal and occipital cortical areas, respectively, cross through the commissure (A2, C2, E2, G2, yellow arrows). Right panel: BOLD effect evoked in the CC of patients with different kind of partial callosotomy by gustatory, tactile, auditory and visual stimulation (respectively B1, D1, F1, H1, green arrows), and sites where fibres connecting fronto-opercular, parietal, temporal and occipital cortical areas, respectively, cross through the commissure (B2, D2, F2, H2, yellow arrows). Numbers are the Talairach coordinates of activation foci. Modified from Fabri and Polonara (2013) and Polonara et al. (2014).

et al., 1984; Risse et al., 1989; Levin et al., 1993; Geschwind et al., 1995; Fabri et al., 1999, 2001; Caillé et al., 2005 see Berlucchi, 2004 and Gazzaniga, 2005, for a review).

Unlike previous works describing a callosal BOLD effect (Tettamanti et al., 2002; Weber et al., 2005; Gawryluk et al., 2011; Mazerolle et al., 2008), the present study did not employ sensory stimuli requiring interhemispheric transfer. Corpus callosum activation was nonetheless observed, suggesting that all information reaching a cortical area is likely transferred to the opposite hemisphere and used to build a continuous representation of the external world.

The callosal topography sketched by DTI and DTT analysis of the data of individual patient confirmed a CC fibre organization, which agrees with that described in previous studies (Abe et al., 2004; Huang et al., 2005; Hofer and Frahm, 2006; Zarei et al., 2006; Chao et al., 2009) and with DTT data obtained in healthy subjects in our lab (Fabri et al., 2014, Fig. 2). Fibres interconnecting prefrontal cortical areas crossed through the anterior part of the CC, if extant; those linking parietal cortical areas crossed through the spared PCB; and those between occipital areas crossed at the level of the splenium, where intact (see also Dougherty et al., 2005; Shimony et al., 2006; Saenz and Fine, 2010). In all tests, the fibres arising from cortical areas activated by each type of stimulus crossed the CC through a region that harboured the respective callosal focus/i.

Very recently, a comprehensive bidirectional callosal connectional atlas between the midsagittal section of the CC and the cerebral cortex of the human brain was built by means of diffusion-weighted imaging tractography, at the highest resolution ever (Xiong et al., 2022). The validity and reproducibility of these estimated topographic maps were proven by comparisons with existing histological data. The callosal topography shown is in agreement with observation reported in the present paper.

3.3. Hemispheric collaboration in higher brain functions

3.3.1. Anatomical imitation

Recent studies from our group were focussed on the anatomical perspective taking in imitating intransitive meaningful gestures, on the mental rotation ability, and on their relationships with the CC.

Functional studies carried out in healthy subjects and callosotomized patients demonstrated that to perform the anatomical imitation also a good interhemispheric connection is necessary (Pierpaoli et al., 2020a, 2021a). In particular, our results indicate that the imitation according to an anatomical criterion seems to require the cooperation of many cortical areas in both hemispheres, sometimes different in the two hemispheres (Pierpaoli et al., 2020a, 2021a). This final observation agrees with previous studies (reviewed in Caspers et al., 2010; Lesourd et al., 2018); it is also consistent with our previous behavioral results obtained in callosotomized patients (Pierpaoli et al., 2018), according to which these patients performed the anatomical imitation less frequently than control subjects, having they more difficulty to engage both hemispheres in a coordinated activity. It seems reasonable to hypothesize, therefore, that the different performances of the patients could be ascribed to the interruption of the CC fibres and consequently to the impossibility for the hemispheres to communicate and cooperate. Since most areas involved in the anatomical imitation are connected through callosal fibres crossing ventral rostral body and ventral anterior midbody or splenium (Chao et al., 2009; Fabri et al., 2014; Polonara et al., 2014), patients lacking callosal fibres from these regions display a lower proportion of anatomical imitation performance (Pierpaoli et al., 2018). Accordingly, in control subjects, an activation focus was observed in the anterior portion of the CC (Fig. 4A).

3.3.2. Mental rotation ability

A subsequent research, designed to identify, by fMRI, the cortical areas activated in during a mental rotation task with human body pictures (Pierpaoli et al., 2021b) confirmed that the lack of callosal fibres, particularly from anterior and/or central body, could impair anatomical imitation performance, although the involved cortical areas could be still activated. This observation is in line with previous studies evidencing that imitation is sustained by a bilateral network (Caspers et al., 2010; Lesourd et al., 2018), and suggesting that the disruption of interhemispheric fibres, other than focal brain lesions, may impair anatomical imitation (Lesourd et al., 2018). The resection of the callosal fibres, interrupting the neural circuit underpinning the anatomical imitation, makes impossible for cortical areas in both hemispheres to communicate and cooperate. Accordingly, in control subjects, an activation focus was observed in the anterior callosal midbody (Fig. 4B).
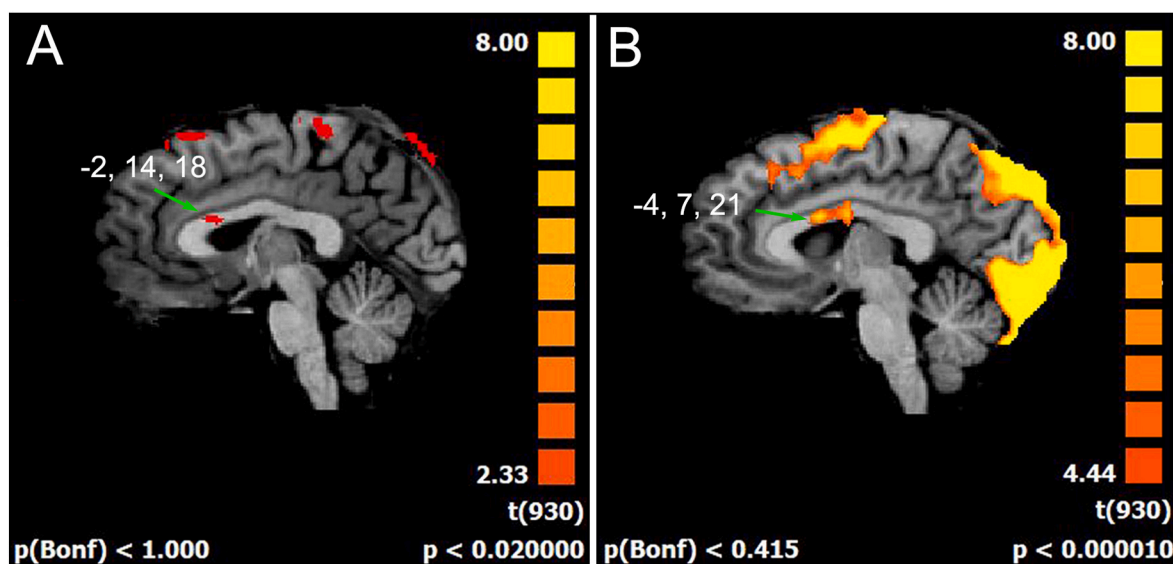

Fig. 4. Activation evoked in the CC during different imagined behaviors. A, during imaging of anatomical imitation of an intransitive gesture an activation focus is visible in the anterior portion of the callosal body, at border with the genu. B, during imaging of a mental rotation operation an activation focus is visible in the anterior portion of the callosal body, slightly posteriorly to that shown in A. The numbers above the arrows in frame B indicate the Talairach coordinates of the activation foci. Anterior pole on the left.

4. Concluding remarks

This review provides a brief outline of key notions and examines neuropsychological and functional studies of the topographic organization of the CC in healthy subjects and in patients with different extents of callosal resection, examined during administration of peripheral sensory stimuli. From this brief review some consideration can be derived.

1. The neuropsychological studies allowed to sketch a subdivision of functions between the different CC regions, confirming a role in interhemispheric transfer of sensory information for the splenium (visual), isthmus (auditory), and posterior midbody (touch), and in the interhemispheric exchange of motor output for central midbody. The anterior CC portion seemed to be involved in more abstract operation, such as attention allocation, mental rotation. The resulting topography was however rather coarse,

2. The functional studies allowed to define a more precise organization, thanks to the possibility to selectively activate the different cortical areas. These studies have documented a BOLD response in various portions of the commissure; they have demonstrated that it can be induced by peripheral stimuli and motor tasks, and have shown CC activation foci are found at discrete sites in relation to the sensory stimulation applied and the motor tasks performed. The resulting functional topographic map agrees with earlier findings.

3. Behavioral and functional studies suggested that the middle-anterior portion of the CC is involved in transfer of higher meaning information (Miller et al., 2010; Pierpaoli et al., 2020a, 2020b, 2021a, 2021b; Fabri et al., 2021) in processing specific stimuli.

Functional activation in the middle-anterior area has sometimes been described in conditions where subjects performed interhemispheric transfer tasks involving crossed and uncrossed conditions (Tettamanti et al., 2002; Weber et al., 2005; Gawryluk et al., 2011; Mazerolle et al., 2008, 2010) which entailed a choice underpinned by a mental operation. Anterior callosal activation has been interpreted as the transfer of a premotor program leading to motor output. Results of recent behavioral and functional research suggest that activation of the anterior midbody is involved in the integration of cortical areas recruited in abstract mental operations. Miller and coworkers (Miller et al., 2010) found that callosotomy patients subjected to resection of the anterior CC were unable to provide moral judgments based on a hypothetical situation; when the same patients were shown a gesture performed by a model standing in front of them and were asked to imitate it, they were unable to do so using an anatomical perspective (Pierpaoli et al., 2018). When, during fMRI session, healthy subjects were asked to mentally imitate intransitive gestures with the same limb used by the model in performing them, callosal activation was detected in the anterior midbody (Pierpaoli et al., 2020a). Altogether, these data suggest that the anterior callosal midbody is involved in mental operations enabling individuals to relate themselves to other subjects, thus also allowing social interaction. The hypothesis is supported by microstructural DTI data showing that this region has a reduced FA value in autistic and psychotic patients, indicating an impaired connectivity that in these patients is paralleled by poor or absent social competences (Frazier and Hardan, 2009; Fujino et al., 2014; Shahab et al., 2017).

These findings, evidencing that different kind of information are transferred through different regions of the CC, characterized by different fiber composition (Aboitiz and Montiel, 2003), are in line with recent hypothesis according to which, in addition to direct stimulation of post-synaptic targets, callosal axons often play a conditional driving or modulatory role. Driving role could be prevalent for primary sensory or motor areas, whereas modulatory for association areas. However, the prevalence of either function is not fixed, but likely depends on task contingencies, as documented by several recent studies (Innocenti et al., 2022).

References

Abe, O., Masutani, Y., Aoki, S., Yamasue, Y., Yamada, H., Kasai, K., Mori, H., Hayashi, N., Masumoto, T., Ohtomo, K., 2004. Topography of the human corpus callosum using diffusion tensor tractography. J. Comput. Assist. Tomogr. 28, 533–539. https://doi.org/10.1097/00004728-200407000-00016.

Aboitiz, F., Montiel, J., 2003. One hundred million years of interhemispheric communication: the history of the corpus callosum. Braz. J. Med. Biol. Res. 36, 409–420. https://doi.org/10.1590/S0100-879X2003000400002.

Aboitiz, F., Scheibel, A.B., Fisher, R.S., Zaidel, E., 1992. Fiber composition of the human corpus callosum. Brain Res. 598, 143–153. https://doi.org/10.1016/0006-8993(92)90179.

Aglioti, S., Tassinari, G., Corballis, M., Berlucchi, G., 2000. Incomplete gustatory lateralization as shown by analysis of taste discrimination after callosotomy. J. Cognit. Neurosci. 1, 238–245. https://doi.org/10.1162/089892900562066.

Aglioti, S.M., Tassinari, G., Fabri, M., Del Pesce, M., Quattrini, A., Manzoni, T., Berlucchi, G., 2001. Taste laterality in the split brain. Eur. J. Neurosci. 13, 195–2001. https://doi.org/10.1046/j.0953-816x.2000.01378.x.

Arguin, M., Lassonde, M., Quattrini, A., Del Pesce, M., Foschi, N., Papo, I., 2000. Divided visuo-spatial attention systems with total and anterior callosotomy. Neuropsychologia 38, 283–291. https://doi.org/10.1016/s0028-3932(99)00077-9.

Barbaresi, P., Fabri, M., Conti, F., Manzoni, T., 1987. D-[3H]aspartate retrograde labelling of callosal and association neurones of somatosensory areas I and II of cats. J. Comp. Neurol. 263, 159–178. https://doi.org/10.1002/cne.902630202.

Barbaresi, P., Fabri, M., Mensà, E., 2014. Characterization of NO producing neurons in the rat corpus callosum. Brain Behav 4, 317–336. https://doi.org/10.1002/brb3.218.

Bentin, S., Sahar, A., Moscovitch, M., 1984. Intermanual information transfer in patients with lesions in the trunk of the corpus callosum. Neuropsychologia 22, 601–611. https://doi.org/10.1016/0028-3932(84)90024-1.

Berlucchi, G., 2004. Some effects of cortical and callosal damage on conscious and unconscious processing of visual information and other sensory inputs. Prog. Brain Res. 144, 79–93. https://doi.org/10.1016/s0079-6123(03)14405-6.

Berlucchi, G., 2012. Frontal callosal disconnection syndromes. Cortex 48, 36–45. https://doi.org/10.1016/j.cortex.2011.04.008.

Berlucchi, G., 2014. Visual interhemispheric communication and callosal connections of the occipital lobes. Cortex 56, 1–13. https://doi.org/10.1016/j.cortex.2013.02.001.

Berlucchi, G., Gazzaniga, M.S., Rizzolatti, G., 1967. Microelectrode analysis of transfer of visual information by the corpus callosum. Arch. Ital. Biol. 105, 583–596.

Bonzano, L., Tacchino, A., Roccatagliata, L., Abbruzzese, G., Mancardi, G.L., Bove, M., 2008. Callosal contributions to simultaneous bimanual finger movements. J. Neurosci. 28, 3227–3233. https://doi.org/10.1523/JNEUROSCI.4076-07.2008.

Caillé, S., Sauerwein, H.C., Schiavetto, A., Villemure, J.-G., Lassonde, M., 2005. Sensory and motor interhemispheric integration after section of different portion of the anterior corpus callosum in nonepileptic patients. Neurosurgery 57, 50–59. https://doi.org/10.1227/01.neu.0000163089.31657.08.

Caspers, S., Zilles, K., Laird, A.R., Eickhoff, S.B., 2010. ALE meta-analysis of action observation and imitation in the human brain. Neuroimage 50, 1148–1167. https://doi.org/10.1016/j.neuroimage.2009.12.112.

Chao, Y.-P., Cho, K.-H., Yeh, C.-H., Chou, K.-H., Chen, J.-H., Lin, C.-P., 2009. Probabilistic topography of human corpus callosum using cytoarchitectural parcellation and high angular resolution diffusion imaging tractography. Hum. Brain Mapp. 30, 3172–3187. https://doi.org/10.1002/hbm.20739.

Clarke, S., Meader, P., Meuli, R., Staub, F., Bellmann, A., Regli, L., deTribolet, N., Assal, G., 2000. Interhemispheric transfer of visual motion information after a posterior callosal lesion: a neuropsychological and fMRI study. Exp. Brain Res. 132, 127–133. https://doi.org/10.1007/s002219900327.

De Guise, E., Del Pesce, M., Foschi, N., Quattrini, A., Papo, I., Lassonde, M., 1999. Callosal and cortical contribution to procedural learning. Brain 122, 1049–1062. https://doi.org/10.1093/brain/122.6.1049.

De Lacoste, M., Kirkpatrick, J.B., Ross, E.D., 1985. Topography of the human corpus callosum. J. Neuropathol. Exp. Neurol. 44, 578–591. https://doi.org/10.1097/00005072-198511000-00004.

Dougherty, R.F., Ben-Shachar, M., Bammer, R., Brewer, A.A., Wandell, B.A., 2005. Functional organization of human occipital-callosal fiber tracts. Proc. Natl. Acad. Sci. USA 102, 7350–7355. https://doi.org/10.1073/pnas.0500003102.

Fabri, M., Manzoni, T., 2004. Glutamic acid decarboxylase immunoreactivity in callosal projecting neurons of cat and rat somatic sensory areas. Neuroscience 123, 557–566. https://doi.org/10.1016/j.neuroscience.2003.09.011.

Fabri, M., Polonara, G., 2013. Functional topography of human corpus callosum: an FMRI mapping study. Neural Plast., e251308 https://doi.org/10.1155/2013/251308.

Fabri, M., Polonara, G., Quattrini, A., Salvolini, U., Del Pesce, M., Manzoni, T., 1999. Role of the corpus callosum in the somatosensory activation of the ipsilateral cerebral cortex: an fMRI study of callosotomized patients. Eur. J. Neurosci. 11, 3893–3994. https://doi.org/10.1046/j.1460-9568.1999.00829.x.

Fabri, M., Polonara, G., Del Pesce, M., Quattrini, A., Salvolini, U., Manzoni, T., 2001. Posterior corpus callosum and interhemispheric transfer of somatosensory information: an fMRI and neuropsychological study of a partially callosotomized patient. J. Cognit. Neurosci. 13, 1071–1079. https://doi.org/10.1162/089892901753294365.

Fabri, M., Del Pesce, M., Paggi, A., Polonara, G., Bartolini, M., Salvolini, U., Manzoni, T., 2005. Contribution of posterior corpus callosum to the interhemispheric transfer of tactile information. Cognit. Brain Res. 24, 73–80. https://doi.org/10.1016/j.cogbrainres.2004.12.003.

Fabri, M., Polonara, G., Mascioli, G., Salvolini, U., Manzoni, T., 2011. Topographical organization of human corpus callosum: an fMRI mapping study. Brain Res. 1370, 99–111. https://doi.org/10.1016/j.brainres.2010.11.039.

Fabri, M., Pierpaoli, C., Barbaresi, P., Polonara, G., 2014. Functional topography of the corpus callosum investigated by DTI and fMRI. World J. Radiol. 6, 895–906. https://doi.org/10.4329/wjr.v6.i12.895.

Fabri, M., Pierpaoli, C., Foschi, N., Polonara, G., 2021. Is the imitative competence an asymmetrically distributed function? Front. Syst. Neurosci. 15, 791520 https://doi.org/10.3389/fnsys.2021.791520.

Frazier, T.W., Hardan, A.Y., 2009. A meta-analysis of the corpus callosum in autism. Biol. Psychiatr. 66, 935–941. https://doi.org/10.1016/j.biopsych.2009.07.022.

Fujino, J., Takahashi, H., Miyata, J., Sugihara, G., Kubota, M., Sasamoto, A., Fujiwara, H., Aso, T., Fukuyam, a H., Murai, T., 2014. Impaired empathic abilities and reduced white matter integrity in schizophrenia. Prog. Neuro-Psychopharmacol. Biol. Psychiatry 48, 117–123. https://doi.org/10.1016/j.pnpbp.2013.09.018.

Funnell, M.G., Corballis, P.M., Gazzaniga, M.S., 2000. Cortical and subcortical interhemispheric interactions following partial and complete callosotomy. Arch. Neurol. 57, 185–189. https://doi.org/10.1001/archneur.57.2.185.

Gawryluk, J.R., D'Arcy, R.C.N., Mazerolle, E.L., Brewer, K.D., Beyea, S.D., 2011. Functional mapping in the corpus callosum: a 4 T fMRI study of white matter. Neuroimage 54, 10–15. https://doi.org/10.1016/j.neuroimage.2010.07.028.

Gazzaniga, M.S., 2000. Cerebral specialization and interhemispheric communication: does the corpus callosum enable the human condition? Brain 123, 1293–1326. https://doi.org/10.1093/brain/123.7.1293.

Gazzaniga, M.S., 2005. Forty-five years of split-brain research and still going strong. Nat. Rev. Neurosci. 6, 653–659. https://doi.org/10.1038/nrn1723.

Gazzaniga, M.S., Freedman, H., 1973. Observations on visual processes after posterior callosal section. Neurology 23, 1126–1130. https://doi.org/10.1212/wnl.23.10.1126.

Geschwind, N., 1965a. Disconnexion syndromes in animals and man. I. Brain 88, 237–294. https://doi.org/10.1093/brain/88.3.585.

Geschwind, N., 1965b. Disconnexion syndromes in animals and man. II. Brain 88, 585–644. https://doi.org/10.1093/brain/88.3.585.

Geschwind, D.H., Iacoboni, M., Mega, M.S., Zaidel, D.W., Cloughesy, T., Zaidel, E., 1995. Alien hand syndrome: interhemispheric motor disconnection due to a lesion in the midbody of the corpus callosum. Neurology 45, 802–808. https://doi.org/10.1212/wnl.45.4.802.

Gonchar, Y.A., Johnson, P.B., Weinberg, R.J., 1995. GABA-immunopositive neurons in rat neocortex with contralateral projections to S-I. Brain Res. 697, 27–34. https://doi.org/10.1016/0006-8993(95)00746-D.

Gordon, H.W., Bogen, J.E., Sperry, R.W., 1971. Absence of disconnection syndrome in two patients with partial section of the neocommissures. Brain 94, 327–336. https://doi.org/10.1093/brain/94.2.327.

Gore, J.C., Li, M., Gaoa, Y., Wu, T.-L., Schilling, K.G., Huang, Y., Mishra, A., Newton, A. T., Rogers, B.P., Chen, L.M., Anderson, A.W., Zhaohua Ding, Z., 2019. Functional MRI and resting state connectivity in white matter – a mini review. Magn. Reson. Imag. 63, 12. https://doi.org/10.1016/j.mri.2019.07.017.

Guillemot, J.P., Richer, L., Prevost, L., Ptito, M., Lepore, F., 1987. Receptive fields properties of somatosensory callosal fibres in the monkey. Brain Res. 402, 293–302. https://doi.org/10.1016/0006-8993(87)90036-9.

Hausmann, M., Corballis, M.C., Fabri, M., 2003. Line bisection in the split brain. Neuropsychology 17, 602–609.

Hausmann, M., Corballis, M.C., Fabri, M., Paggi, A., Lewald, J., 2005. Sound lateralization in subjects with callosotomy, callosal agenesis, or hemispherectomy. Cognit. Brain Res. 25, 537–546.

Higo, S., Akashi, K., Sakimura, K., Tamamaki, N., 2009. Subtypes of GABAergic neurons project axons in the neocortex. Front. Neuroanat. 3, 25. https://doi.org/10.3389/neuro.05.025.2009.

Hofer, S., Frahm, J., 2006. Topography of the human corpus callosum revisited. Comprehensive fiber tractography using diffusion tensor magnetic resonance imaging. Neuroimage 32, 989–994. https://doi.org/10.1016/j.neuroimage.2006.05.044.

Hofer, S., Merboldt, K.-D., Tammer, R., Frahm, J., 2008. Rhesus monkey and human share a similar topography of the corpus callosum as revealed by diffusion tensor MRI in vivo. Cerebr. Cortex 18, 1079–1084. https://doi.org/10.1093/cercor/bhm141.

Huang, H., Zhang, J., Jiang, H., Wakana, S., Poetscher, L., Miller, M.I., Van Zijl, P.C.M., Hillis, A.E., Wytik, R., Mori, S., 2005. DTI tractography based parcellation of white matter: application to mid-sagittal morphology of corpus callosum. Neuroimage 26, 195–205. https://doi.org/10.1016/j.neuroimage.2005.01.019.

Hubel, D.H., Wiesel, T.N., 1967. Cortical and callosal connections concerned with the vertical meridian of visual fields in the cat. J. Neurophysiol. 30, 1561–1573. https://doi.org/10.1152/jn.1967.30.6.1561.

Innocenti, G.M., 1986. General organization of callosal connections in the cerebral cortex. In: Jones, E.G., Peters, A. (Eds.), Cerebral Cortex. Plenum Press, New York, pp. 291–353 vol. 5.

Innocenti, G.M., Manzoni, T., Spidalieri, G., 1972. Cutaneous receptive fields of single fibres of the corpus callosum. Brain Res. 40, 507–512. https://doi.org/10.1016/0006-8993(72)90153-9.

Innocenti, G.M., Manzoni, T., Spidalieri, G., 1974. Patterns of the somesthetic messages transferred through the corpus callosum. Exp. Brain Res. 19, 447–466. https://doi.org/10.1007/BF00236110.

Innocenti, G.M., Schmidt, K., Milleret, C., Fabri, M., Knyazeva, M.G., Battaglia-Mayer, A., Aboitiz, F., Ptito, M., Caleo, M., Marzi, C.A., Barakovic, M., Lepore, F., Caminiti, R., 2022. The functional characterization of callosal connections. Prog. Neurobiol. 208, 102186 https://doi.org/10.1016/j.pneurobio.2021.102186.

Koch, G., Cercignani, M., Bonnì, S., Giacobbe, V., Bucchi, G., Versace, V., Caltagirone, C., Bozzali, M., 2011. Asymmetry of parietal interhemispheric connections in humans. J. Neurosci. 31, 8967–8975. https://doi.org/10.1523/JNEUROSCI.6567-10.2011.

Lesourd, M., Osiurak, F., Baumard, J., Bartolo, A., Vanbellingen, T., 2018. Cerebral correlates of imitation of intransitive gestures: an integrative review of neuroimaging data and brain lesion studies. Neurosci. Biobehav. Rev. 95, 44–60. https://doi.org/10.1016/j.neubiorev.2018.07.019.

Levin, H.S., Mattson, A.J., Levander, M., Lindquist, C.E.H., Simard, J.M., Guinto, F.C., Lilly, M.A., Eisenberg, H.M., 1993. Effects of transcallosal surgery on interhemispheric transfer of information. Surg. Neurol. 40, 65–74. https://doi.org/10.1016/0090-3019(93)90174-y.

Logothetis, N.K., Pauls, J., Augath, M., Trinath, T., Oeltermann, A., 2001. Neurophysiological investigation of the basis of the fMRI signal. Nature 412, 150–157. https://doi.org/10.1038/35084005.

Malobabić, S., Bogdanović, D., Drekić, D., 1984. On the neurons with dendrites intermingling with the fibers of the human corpus callosum: a Golgi picture. Gegenbaurs Morphol. Jahrb. 130, 557–564.

Manzoni, T., 1998. The cerebral ventricles, the animal spirits and the dawn of brain localization of function. Arch. Ital. Biol. 136, 103–152.

Manzoni, T., 2011. Fibre associative e commisurali, 5-5. In: Corteccia Cerebrale e funzioni cognitive. Ventitré secoli di storia. Cap, Roma, pp. 230–232. Carocci.

Mascioli, G., Berlucchi, G., Pierpaoli, C., Salvolini, U., Barbaresi, P., Fabri, M., Polonara, G., 2015. Functional MRI cortical activations from unilateral tactile-taste stimulations of the tongue. Physiol. Behav. 151, 221–229. https://doi.org/10.1016/j.physbeh.2015.07.031.

Mazerolle, E.L., D'Arcy, R.C.N., Song, X., Beyea, S.D., 2008. Detecting fMRI activation in white matter: interhemispheric transfer across the corpus callosum. BioMed Central Neurosci 9, 84–94. https://doi.org/10.1186/1471-2202-9-84.

Mazerolle, E.L., Beyea, S.D., Gawryluk, J.R., Brewer, K.D., Bowen, C.V., D'Arcy, R.C., 2010. Confirming white matter fMRI activation in the corpus callosum: co-localization with DTI tractography. Neuroimage 50, 616–621. https://doi.org/10.1016/j.neuroimage.2009.12.102.

Men, W., Falk, D., Sun, T., Chen, W., Li, J., Yin, D., Zang, L., Fan, M., 2014. The corpus callosum of Albert Einstein's brain: another clue to his high intelligence? Brain 137, e268. https://doi.org/10.1093/brain/awt252.

Meyer, B.U., Roricht, S., Grafin von Einsiedel, H., Kruggel, F., Weindi, A., 1995. Inhibitory and excitatory interhemispheric transfers between motor cortical areas in normal humans and patients with abnormalities of the corpus callosum. Brain 118, 429–440. https://doi.org/10.1093/brain/118.2.429.

Miller, M.B., Sinnott-Armstrong, W., Young, L., King, D., Paggi, A., Fabri, M., Polonara, G., Gazzaniga, M.S., 2010. Abnormal moral reasoning in complete and partial callosotomy patients. Neuropsychologia 48, 2215–2220. https://doi.org/10.1016/j.neuropsychologia.2010.02.021.

Mosier, K., Bereznaya, I., 2001. Parallel cortical networks for volitional control of swallowing in humans. Exp. Brain Res. 140, 280–289. https://doi.org/10.1007/s002210100813.

O'Sullivan, M., Jones, D.K., Summers, P.E., Morris, R.G., Williams, S.C., Markus, H.S., 2001. Evidence for cortical "disconnection" as a mechanism of age-related cognitive decline. Neurology 57, 632–638.

Oldfield, R.C., 1971. The assessment and analysis of handedness: the Edinburgh inventory. Neuropsychologia 9, 97–113.

Oliveira, R., Pelentritou, A., Di Domenicantonio, G., De Lucia, M., Lutti, A., 2022. In vivo estimation of axonal morphology from magnetic resonance imaging and electroencephalography data. Front. Neurosci. 16, 874023 https://doi.org/10.3389/fnins.2022.874023.

Omura, K., Tsukamoto, T., Kotani, Y., Ohgami, Y., Minami, M., Inoue, Y., 2004. Different mechanisms involved in interhemispheric transfer of visuomotor information. Neuroreport 15, 2707–2711.

Pandya, D.N., Seltzer, B., 1986. The topography of commissural fibers. In: Leporé, F., Ptito, M., Jasper, H.H. (Eds.), Two Hemispheres-One Brain: Functions of the Corpus Callosum. Alan Liss, New York, pp. 47–73.

Pandya, D.N., Karol, E.A., Heilbronn, D., 1971. The topographical distribution of interhemispheric projections in the corpus callosum of the rhesus monkey. Brain Res. 32, 31–43. https://doi.org/10.1016/0006-8993(71)90153-3.

Passamonti, C., Zamponi, N., Foschi, N., Trignani, R., Luzi, M., Cesaroni, E., Provinciali, L., Scerrati, M., 2014. Long-term seizure and behavioral outcomes after corpus callosotomy. Epilepsy Behav. 41, 23–99. https://doi.org/10.1016/j.yebeh.2014.08.130.

Paul, L.K., 2011. Developmental malformation of the corpus callosum: a review of typical callosal development and examples of developmental disorders with callosal involvement. J. Neurodev. Disord. 3, 3–27. https://doi.org/10.1007/s11689-010-9059-y.

Pierpaoli, C., Ferrante, L., Berlucchi, G., Manzoni, T., Fabri, M., 2014. Anatomical or mirror – mode imitation? A behavioral approach. Arch. Ital. Biol. 152, 20–31.

Pierpaoli, C., Foschi, N., Cagnetti, C., Ferrante, L., Manzoni, T., Polonara, G., Fabri, M., 2018. Imitation strategies in callosotomeized patients. Arch. Ital. Biol. 156, 12–26. https://doi.org/10.12871/00039829201812.

Pierpaoli, C., Fabri, M., Polonara, G., 2020a. Cortical activation during imitative behavior: an fMRI study. J. Syst. Integr. Neurosci. 7, 1–12. https://doi.org/10.15761/JSIN.1000226.

Pierpaoli, C., Ferrante, L., Foschi, N., Lattanzi, S., Sansonetti, R., Polonara, G., Mari, M., Nardi, B., Fabri, M., 2020b. Mental rotation ability: right or left hemisphere competence? what we can learn from callosotomized and psychotic patients. Symmetry 12, 1137. https://doi.org/10.3390/sym12071137.

Pierpaoli, C., Foschi, N., Fabri, M., Polonara, G., 2021a. Cortical activation during imitative behavior: an fMRI study in callosotomized patients. J. Syst. Integr. Neurosci. 7, 1–15. https://doi.org/10.15761/JSIN.1000253.

Pierpaoli, C., Ghoushi, M., Foschi, N., Lattanzi, S., Fabri, M., Polonara, G., 2021b. Cortical activation in mental rotation and the role of the corpus callosum: observations in healthy subjects and split-brain patients. Symmetry 13, 1953. https://doi.org/10.3390/sym13101953.

Pollmann, S., Maertens, M., Von Cramon, D.Y., Lepsien, J., Hugdahl, K., 2002. Dichotic listening in patients with splenial and nonsplenial callosal lesions. Neuropsychology 16, 56–64. https://doi.org/10.1037/0894-4105.16.1.56.

Polonara, G., Fabri, M., Manzoni, T., Salvolini, U., 1999. Localization of the first and second somatic sensory areas in human cerebral cortex with fMRI. AJNR, American Journal of NeuroRadiology 20, 199–205.

Polonara, G., Masciuli, G., Foschi, N., Salvolini, U., Pierpaoli, C., Manzoni, T., Fabri, M., Barbaresi, P., 2014. Further evidence for the topography and connectivity of the corpus callosum: an FMRI study of patients with partial callosal resection. J. Neuroimmunol. 25, 465–473. https://doi.org/10.1111/jon.12136.

Prete, G., Laeng, B., Fabri, M., Foschi, N., Tommasi, L., 2015a. Right hemisphere or valence hypothesis, or both? The processing of hybrid faces in the intact and callosotomized brain. Neuropsychologia 68, 94–106. https://doi.org/10.1016/j.neuropsychologia.2015.01.002.

Prete, G., D'Ascenzo, S., Laeng, B., Fabri, M., Foschi, N., Tommasi, L., 2015b. Conscious and unconscious processing of facial expressions: evidence from two split-brain patients. J. Neuropsychol. 9, 45–63. https://doi.org/10.1111/jnp.12034.

Raybaud, C., 2010. The corpus callosum, the other great forebrain commissures, and the septum pellucidum: anatomy, development and malformation. Neuroradiology 52, 447–477. https://doi.org/10.1007/s00234-010-0696-3.

Revishchin, A.V., Okhotin, V.E., Korochkin, L.I., Pavlova, G.V., 2010. A new population of calretinin-positive cells, presumptively neurons, with polymorphous spines in the mouse forebrain. Neurosci. Behav. Physiol. 40, 541–552. https://doi.org/10.1007/s11055-010-9295-3.

Riederer, B.M., Berbel, P., Innocenti, G.M., 2004. Neurons in the corpus callosum of the cat during postnatal development. Eur. J. Neurosci. 19, 2039–2046. https://doi.org/10.1111/j.1460-9568.2004.03305.x, 2004.

Risse, G.L., Gates, J., Lund, G., Maxwell, R.C., Rubens, A., 1989. Interhemispheric transfer in patients with incomplete section of the corpus callosum. Arch. Neurol. 46, 437–443. https://doi.org/10.1001/archneur.1989.00520400097026.

Rockland, K.S., Nayyar, N., 2012. Association of type I neurons positive for NADPH-diaphorase with blood vessels in the adult monkey corpus callosum. Front. Neural Circ. 6, e4. https://doi.org/10.3389/fncir.2012.00004.

Saenz, M., Fine, I, 2010. Topographic organization of V1 projections through the corpus callosum in humans. Neuroimage 52, 1224–1229. https://doi.org/10.1016/j.neuroimage.2010.05.060.

Schulte, T., Sullivan, E.V., Müller-Oehring, E.M., Adalsteinsson, E., Pfefferbaum, A., 2005. Corpus callosal microstructural integrity influences interhemispheric processing: a Diffusion Tensor Imaging study. Cerebr. Cortex 15, 1384–1392. https://doi.org/10.1093/cercor/bhi020.

Shahab, S., Stefanik, L., Foussias, G., Lai, M.-C., Anderson, K.K., Voineskos, A.N., 2017. Sex and diffusion tensor imaging of white matter in schizophrenia: a systematic review plus meta-analysis of the corpus callosum. Schizophr. Bull. 44, 203–221. https://doi.org/10.1093/schbul/sbx049.

Shimony, J.S., Burton, H., Epstein, A.A., McLaren, D.G., Sun, S.W., Snyder, A.Z., 2006. Diffusion tensor imaging reveals white matter reorganization in early blind humans. Cerebr. Cortex 16, 1653–1661. https://doi.org/10.1093/cercor/bhj102.

Stancak Jr., A., Lucking, C.H., Kristeva-Feige, R., 2000. Lateralization of movement related potentials and the size of corpus callosum. Neuroreport 11, 329–332. https://doi.org/10.1097/00001756-200002070-00021.

Sugishita, M., Otomo, K., Yamazaki, K., Shimizu, H., Yoshioka, M., Shinohara, A., 1995. Dichotic listening in patients with partial section of the corpus callosum. Brain 118, 417–427. https://doi.org/10.1093/brain/118.2.417.

Talairach, J., Tournoux, P., 1988. Co-Planar Stereotaxic Atlas of the Human Brain. Thieme, Stuttgart.

Tettamanti, M., Paulesu, E., Scifo, P., Maravita, A., Fazio, F., Perani, D., Marzi, C.A., 2002. Interhemispheric transmission of visuomotor information in humans: fMRI evidence. J. Neurophysiol. 88, 1051–1058. https://doi.org/10.1152/jn.2002.88.2.1051.

Volpe, B.T., Sidtis, J.J., Holtzman, J.D., Wilson, D.H., Gazzaniga, M.S., 1982. Cortical mechanisms involved in praxis: observations following partial and complete section of the corpus callosum in man. Neurology 32, 645–650. https://doi.org/10.1212/wnl.32.6.645.

Wahl, M., Lauterbach-Soon, B., Hattingen, E., Jung, P., Singer, O., Volz, S., Klein, J.C., Steinmetz, H., Ziemann, U., 2007. Human motor corpus callosum: topography, somatotopy, and link between microstructure and function. J. Neurosci. 27, 12132–12138. https://doi.org/10.1523/JNEUROSCI.2320-07.2007.

Weber, B., Treyer, V., Oberholzer, N., Jaermann, T., Boesiger, P., Brugger, P., Regard, M., Buck, A., Savazzi, S., Marzi, C.A., 2005. Attention and interhemispheric transfer: a behavioural and fMRI study. J. Cognit. Neurosci. 17, 113–123. https://doi.org/10.1162/0898929052880002.

Westerhausen, R., Karud, C.M.R., 2018. Callosotomy affects performance IQ: a meta-analysis of individual participant data. Neurosci. Lett. 665, 43–47. https://doi.org/10.1016/j.neulet.2017.11.040.

Witelson, S., 1989. Hand and sex differences in the isthmus and genu of the human corpus callosum. A postmortem morphological study. Brain 112, 799–835. https://doi.org/10.1093/brain/112.3.799.

Xiong, Y., Yang, L., Wang, L., Zhao, C., Luo, J., Wu, D., Ouyang, Y., Thiebaut de Schotten, M., Gong, G., 2022. Population-based Cortical Mapping of Callosal Connections in the Human Brain. https://doi.org/10.21203/rs.3.rs-2210117/v1.

Yang, L., Zhao, C., Xiong, Y., Zhong, S., Wu, D., Peng, S., Thiebaut de Schotten, M., Gong, G., 2022. Callosal fiber length scales with brain size according to functional lateralization, evolution, and development. J. Neurosci. 42, 3599–3610. https://doi.org/10.1523/JNEUROSCI.1510-21.2022.

Zarei, M., Johansen-Berg, H., Smith, S., Ciccarelli, O., Thompson, A.J., Matthews, P.M., 2006. Functional anatomy of interhemispheric cortical connections in the human brain. J. Anat. 209, 311–320. https://doi.org/10.1111/j.1469-7580.2006.00615.x.